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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,121	FELDING ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,21,23-29 and 31-38* is/are pending in the application.

4a) Of the above claim(s) *26,27 and 31-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,21,23-25,28,29 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/1/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

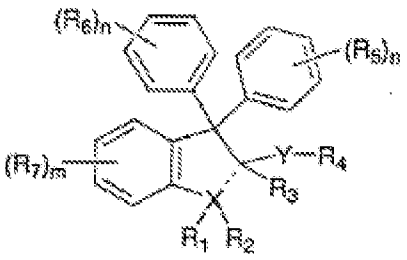
DETAILED ACTION

Claims 1, 4-8, 21, 23-29, and 31-38 are presented for examination

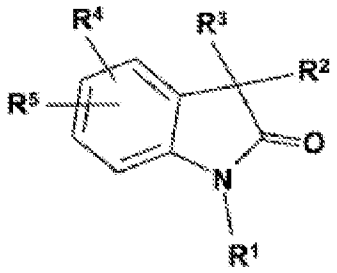
Applicant's claim amendments, filed 6/9/2009, have been received and entered. Accordingly, claims 2-3 and 11 are cancelled and claim 38 is newly added.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1, 4-8, 21, 23-29, and 38) and the species represented by 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one (i.e., "Compound 41"; the compound of Formula I wherein R1 and R2 are fluorine, R3 and R4 are hydrogen, and X1 and X2 are hydroxyl) in the reply filed on 6/9/2009 is acknowledged. The traversal is on the ground(s) that at least Groups I, XIII, and XV share an inventive concept and do not place an undue search burden on the Examiner. This is not found persuasive because as discussed in the Requirement for Restriction mailed 5/15/2009, the compounds recited in the instant claims were known and/or suggested in the art prior to Applicant's invention and thus do not meet the requirement of an inventive concept. For example, WO 99/26611 teaches compounds of Formula (I):



and WO 03/078394 teaches compounds of Formula (I):



Formula I

The compounds disclosed in WO 99/26611 and WO 03/078394 obviate the compounds recited in the instant claims, *e.g.*, compounds of Formula (I) as recited in claim 1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 26-27 are withdrawn from further consideration are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species and claims 31-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/9/2009.

Accordingly, claims 1, 4-8, 21, 23-25, 28-29 and 38 are presently under examination on their merits and are subject to the rejections and/or objections set forth below.

Priority

This application is a U.S. national phase application under 35 U.S.C. § 371 of International Patent Application No. PCT/DK2005/000244, filed April 8, 2005, and claims the benefit of Danish Application No. 2004 00576, filed April 8, 2004; Danish Application No. 2004 00693, filed May 1, 2004; Danish Application No. 2004 01153, filed July 27, 2004; and Danish Application No. 2004 01216, filed August 11, 2004.

The earliest effective U.S. filing date afforded the claimed invention is **April 8, 2005**.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 6/1/2007. The Examiner has considered the references cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 recites the limitation "the medicament" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-8, 21, 23-25, 28-29 and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to methods of using compounds of Formula (I), (IIa), or (IIb) and pharmaceutically acceptable salts and prodrugs thereof.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claims indicates that these claims are drawn to a generic genus, *i.e.*, generic prodrugs of compounds of Formula (I), (IIa), or (IIb).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(i), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

The specification discloses at page 11, lines 3-7 that the term “prodrug” refers to a derivative of a compound of the Formula (I) which upon exposure to physiological conditions will liberate a compound of the formula (I) which then will be able to exhibit the desired

biological action. Examples of prodrugs are esters (carboxylic acid ester, phosphate esters, sulphuric acid esters, etc.), acid labile ethers, acetals, ketals, etc.

There is not a single example disclosed that is within the scope of the claimed genus, *i.e.* a prodrug of Formula (I), (IIa), or (IIb). In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a generic genus of compounds, *i.e.*, generic prodrugs of Formula (I), (IIa), or (IIb) purported to liberate a compound of the formula (I) which then will be able to exhibit anticancer activity. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 1, 4-8, 21, 23-25, 28-29 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making compounds of Formula (I), (IIa), and (IIb), does not reasonably provide enablement for making a "*prodrug*" of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 1, 24, and 25 and claims dependent therefrom recite a "prodrug" of compounds represented by Formula (I), (IIa), and (IIb). The term "prodrug" covers just about any ester, amide, phosphate, sulfate having an infinite combination of functional groups, rings, substituents, etc., and could drastically alter the structure of the parent compound. Thus, the scope of the above claims are unduly broad.

The amount of direction or guidance presented: Although the specification briefly defines what a "prodrug" is (see page 11, lines 3-7), it does not provide working examples to guide the skilled chemist to select a particular ester, amide, phosphate or sulfate for a particular site on the parent compound in order to obtain a "prodrug". Thus, the specification fails to provide sufficient enablement for making a "prodrug" of the claimed compounds.

The state of the prior art: Although it is not unusual to expect a "prodrug" of a compound, the process for selecting a particular ester, amide, phosphate, sulfate, etc. for making a prodrug is not standard for all drugs. For the claimed compounds, there is no reference teaching possible prodrugs. Thus, the state of the prior art does not support the broad scopes of the above claims. Thus, the state of the prior art does not support the broad scope of the above claims.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select a particular "prodrug" for each compound from the large Markush group of Formulas (I), (IIa), and (IIb), with no guidance or direction from the instant disclosure. Not only has one to determine an IC_{50} value, but also *in vivo* activity to establish an LD_{50}, therapeutic index and active metabolites for each "prodrug". Given a large Markush group of the three claimed formulae, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a prodrug requires three criteria: (1) the "prodrug" must be biologically inactive; (2) the "prodrug" must be metabolized into the active drug at a physiologically meaningful concentration; (3) the active drug must still have the intended biological activity. Many prodrugs produce additional active metabolites (*in vivo*) that do not have the same chemical structure of the intended drug. Thus, the process of making a prodrug is highly unpredictable due to many unknown *in vivo* factors as well as uncertain numbers of active metabolites with potential adverse effects.

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make the hundreds of thousands of compounds covered by the claimed "prodrug" of compounds represented by formula in the above claims.

Claims 1, 4-8, 21, 23-25, 28-29 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a mammal *suffering from* cancer, does not reasonably provide enablement for treating a mammal *susceptible to* cancer (i.e., prevention). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 1, 24, and 25 and claims dependent therefrom recite methods of treating mammals suffering from or being susceptible to cancer comprising administering to the mammal a compound of Formula (I), (IIa), or (IIb). The Examiner is interpreting the claimed "being susceptible to cancer" to indicate a population of mammals that do not have cancer wherein the recited "treating" results in prevention of cancer in the mammal.

The amount of direction or guidance presented: Although the specification demonstrates that two compounds of the invention (Compound 3 and Compound 41) have in vivo tumor growth inhibitory activity, there is no working example relating to the claimed treatment of a mammal susceptible to cancer wherein treatment with a compound of the invention prevents cancer from occurring in the mammal. Applicants offer no guidance or direction with regard to determining what mammals are "susceptible to cancer" and would thus be in need of the claimed treatment.

The state of the prior art: The prevention of cancer in mammals, especially humans, is not recognized in the art as being feasible in view of the present state of the art in oncology. Although there are hundreds of chemotherapeutic agents that are used in the clinic to treat cancer, such compounds are not presently capable of generally preventing the cancers they are effective to treat.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to what compound(s) from the large Markush group of Formulas (I), (IIa), and (IIb) would be effective to prevent cancer in susceptible mammals, with no guidance or direction from the instant disclosure. Not only has one to determine a compound effective to inhibit tumor growth of a given cancer, but additionally to monitor a susceptible mammal provided the compound for an indeterminate time period to verify that no cancer develops in the treated mammal. Given a large Markush group of the three claimed formulae, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of identifying and treating a susceptible mammal with a compound of the invention to determine whether the compound effectively prevents cancer development in the mammal is unpredictable, especially in view of the scope of the claimed compounds and limited testing carried out by Applicants.

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make and test the hundreds of thousands of compounds covered by the claimed compounds represented by formula in the above claims for efficacy in generally preventing cancer in mammals.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

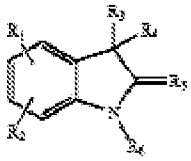
Claims 1, 4-8, 21, 23-25, 28, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Halperin *et al.*** (US 2007/0099976 A1; Published May 3, 2007; Filed Aug. 9, 2006; U.S. Priority claimed to Feb. 13, 2004) (newly cited).

Halperin *et al.* qualifies as prior art under 35 U.S.C. 102(e) because the earliest effective U.S. filing date of US 2007/0099976 A1 is February 13, 2004, which predates Applicant's

earliest effective U.S. filing date of April 8, 2005 and Applicant's earliest foreign priority claim (April 8, 2004).

The instant claims recite methods of treating a mammal suffering from or being susceptible to cancer comprising administering to the mammal a compound of Formula (I) (claim 1), Formula (IIa) (claim 24), or Formula (IIb) (claim 25).

The cited prior art discloses compounds having the formula:



wherein the substituents defined in the reference obviate the claimed compounds of Formula (I) (claim 1), Formula (IIa) (claim 24), and Formula (IIb) (claim 25) (page 3, [0025] to page 6, [0050]; Tables 1-3 and 6-7). For example, Compound 1259 in Table 6 of the cited reference reads on the compounds of Formulas (IIa) and (IIb) in claims 24 and 25 when X^1 and X^2 are OH and R^1, R^2, and R^3 are hydrogen.

With regard to claims 4 and 21, Halperin *et al.* disclose compounds wherein R^1 is halogen or C_{1-6}-alkyl (Table 1, Compounds 1207, 1267, 1268) or wherein R^1 is hydrogen (Table 6, all compounds).

With regard to claim 5, Halperin *et al.* disclose compounds wherein R^2 is halogen or C_{1-6}-alkyl (Table 1, Compounds 1271 and 1273) or wherein R^2 is hydrogen (Table 6, all compounds).

With regard to claim 6, Halperin *et al.* disclose compounds wherein R^3 is halogen (Table 1, Compounds 1205, 1206, 1207, 1350) or wherein R^3 is hydrogen (Table 6, all compounds).

With regard to claim 7, Halperin *et al.* disclose compounds wherein R^4 is hydrogen (see compounds disclosed in Tables 1 and 6).

With regard to claims 8 and 38, Halperin *et al.* disclose compounds wherein X^1 and X^2 are independently hydroxy and/or NMe_2 (Table 6, compounds 1259 and 1262).

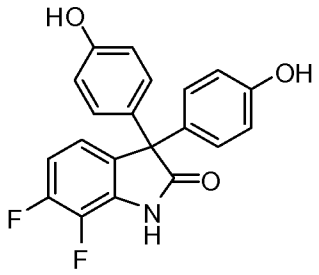
With regard to claim 23, Halperin *et al.* disclose compounds wherein R^1 is halogen or C_{1-4}-alkyl, R^2 is hydrogen or halogen, and R^3 is hydrogen, halogen, or C_{1-4} alkyl, where R^2 and R^3 are not both hydrogen (Table 1, compounds 1205, 1206, 1269, 1271, 1273, and 1350).

The instantly elected specie, 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one (*i.e.*, "Compound 41"; the compound of Formula I wherein R^1 and R^2 are fluorine, R^3 and R^4 are hydrogen, and X^1 and X^2 are hydroxyl) is obviated by the disclosure in the cited prior art of compounds having 3,3-bis-(4-hydroxy-phenyl) substituents (Compound 1259 in Table 6) and the disclosure in the reference of compounds substituted at the 4, 5, 6, or 7 position of the phenyl ring with halogens, including fluorine (Table 1). The inventors disclose that in compounds having the formula recited above, R^1 and R^2 can both be "halogen" (page 3, [0025]).

With regard to the claimed treatment methods, Halperin *et al.* disclose that the compounds of the invention are useful for treating cellular proliferative diseases (Abstract), including cancer, by administering the disclosed compounds to a mammal (page 2, [0011]; page 2, [0019]; Figure 5; claims 18 and 19).

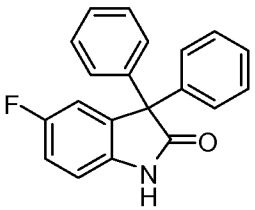
Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a compound disclosed in Halperin et al. and test this compound for anticancer activity. The skilled artisan would have been imbued with at least a reasonable expectation of success in such an endeavor in light of the extensive direction and guidance provided by Halperin, including *in vitro* Ca^{2+} release from intracellular stores, phosphorylation of eIF2α, inhibition of A529 lung cancer cell growth, and *in vivo* antitumor activity (squamous cell carcinoma) of a compound disclosed therein (Compound 1181).

Applicant's elected compound differs from compounds explicitly disclosed in the cited prior art in that the compound contains 3,3-bis-(4-hydroxy-phenyl) substituent and 6,7-difluoro substituent:

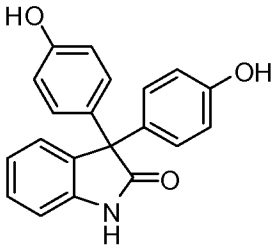


Elected Compound

Of the species explicitly disclosed in Halperin, the following compounds are closest in structure to Applicant's elected compound:

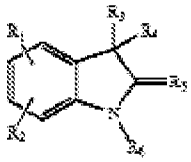


Halperin Compound 1350 (Table 1)



Halperin Compound 1259 (Table 6)

Thus, to arrive at Applicant's elected compound, 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one, one skilled in the art must substitute the 1,3-dihydro-indol-2-one with fluorine groups at the 6 and 7 positions of the phenyl ring in compound 1259 or move the fluorine at position 5 of the phenyl ring in compound 1350 to the 6-position, add an additional fluorine at the 7-position, and add hydroxy groups to the 4-position of the two 3,3-bis phenyl rings in compound 1259. Given the disclosure Halperin *et al.*, who teach that compounds having the formula



can be substituted at both the R_1 and R_2 positions with a "halogen", one skilled in the art could readily envision making the changes required to arrive at the instantly elected compound. This is especially true given the fact that Halperin et al. disclose compounds having 3,3-bis-(4-hydroxy-phenyl) groups as well as compounds having halogen substituents on the 1,3-dihydro-indol-2-one phenyl ring (see Tables 1 and 6).

Halperin *et al.* teach that a multitude of compounds of the invention have in vitro activity in releasing Ca^{2+} from intracellular stores, phosphorylating eIF2α, and inhibiting A529 lung cancer cell growth. Halperin *et al.* additionally demonstrate the in vivo anticancer activity of one compound of the invention (compound 1181). As such, it would not take undue experimentation to make the instantly elected 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one and test it for activity in releasing Ca^{2+} from intracellular stores, phosphorylating eIF2α, and inhibiting cancer cell growth *in vitro*.

Applicant's results have been carefully considered but are not persuasive, a priori, that an unexpected result has been demonstrated. Applicant's elected compound, 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one (Compound 41) was tested for in vivo tumor growth inhibition of breast cancer tumors (see Figures 16 and 17). However, Halperin et al. disclose that compounds of their invention, which encompass the instantly elected compound as discussed above, are effective in treating cancer, including breast cancer (page 7, [0052]). As such, in the absence of a comparison between 6,7-difluoro-3,3-bis-(4-hydroxy-phenyl)-1,3-dihydro-indol-2-one (elected compound) and other compounds disclosed in Halperin et al., Applicant's results are not demonstrative of an unexpected result.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Halperin *et al.*** (US 2007/0099976 A1; Published May 3, 2007; Filed Aug. 9, 2006; U.S. Priority claimed to Feb. 13, 2004) as applied to claims 1, 4-8, 21, 23-25, 28, and 38 above, and further in view of **Brugnara *et al.*** (WO 99/26611; Published June 3, 1999).

Halperin *et al.* teach as applied *supra*. Such teachings are herein incorporated by reference. Claim 29 differs from Halperin *et al.* in that the primary reference does not teach or suggest a treatment method further comprising one or more other chemotherapuetic agents.

However, Brugnara *et al.* teach a genus of 3,3-diphenyl indanone compounds structurally related to the compounds disclosed in Halperin *et al.* which are also useful in the treatment of cancer (Abstract; page 6, line 2 to page 7, line 23; page 8, line 26 to page 9, line 3; page 18, line 33 to page 19, line 21). With regard to claim 29, Brugnara *et al.* teach that when administered to a patient undergoing cancer treatment, the compounds may be administered in cocktails containing other anti-cancer agents (page 31, lines 34-37; page 32, lines 4-22).

As such, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made that the compounds disclosed in Halperin *et al.* as anticancer agents, which compounds encompass the instantly elected compound, could be predictably combined with other chemotherapeutic agents as suggested and motivated by Brugnara *et al.* Such combination chemotherapy is routine in the art of oncology and the skilled artisan would expect that such combinations would be effective in the treatment of cancer.

Conclusion

Claims 1, 4-8, 21, 23-25, 28-29 and 38 are properly rejected.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/James D Anderson/
Examiner, Art Unit 1614